CLAIMS

What is claimed is:

1. A substantially non-immunogenic prosthetic device for implantation into a vertebrate subject in a region disposed between and connecting two of the subject's bones, comprising a biocompatible glycosidase-treated matrix material, wherein the device matrix is adapted to have an *in vivo* an outer surface contour substantially the same as that of a region disposed between and connecting two of the subject's bones.

2. The device of claim 1, wherein the glycosidase is a galactosidase.

3. The device of claim 2, wherein the galactosidase is an α-galactosidase.

4. The device of claim 1, wherein the matrix material has a plurality of first surface carbohydrate moieties substantially removed.

5. The device of claim 1, wherein the matrix material is produced by:
   (a) removing at least a portion of a soft tissue from a non-human animal to provide a matrix material for the prosthetic device;
   (b) washing the matrix material in water and alcohol;
   (c) subjecting the matrix material to a cellular disruption treatment; and
   (d) digesting the matrix material with a glycosidase to remove substantially a plurality of first surface carbohydrate moieties from the matrix material.

6. The device of claim 1, further comprising a cross-linking agent.

7. The device of claim 6, wherein the cross-linking agent is selected from the group consisting of glutaraldehyde, formaldehyde, biocompatible bifunctional aldehydes, carbodiimides, hexamethylene diisocyanate, bis-ionidates, polyglycerol polyglycidyl ether, glyoxal, bisimidates, adipyl chloride and mixtures thereof.

8. The device of claim 1, further comprising cross-links between at least a portion of the matrix material.

9. The device of claim 8, wherein the cross-links are dispersed substantially non-uniformly throughout the matrix.

10. The device of claim 8, wherein the cross-links are formed by a chemical cross-linking agent.

11. The device of claim 8, wherein the cross-links having relatively high density at tip regions of the device and relatively low density at central regions of the device.

12. The device of claim 8, wherein the molecular weight of the molecular cross-links is within the range of about 800-60,000 daltons.

13. The device of claim 8, wherein the cross-links comprises at least one of the group of glycosaminoglycan molecules consisting of chondroitin 4-sulfate; chondroitin 6-sulfate; keratin sulfate; dermatan sulfate; and hyaluronic acid.

14. The device of claim 1,

(a) wherein the matrix material comprises collagen and glycosaminoglycan cross-links, and

(b) wherein the glycosaminoglycan cross-links are present at a density less than about 0.95 and greater than about 0.50 cross-link/collagen ratio.

15. The device of claim 1, wherein the device matrix establishes an at least partially bioresorbable scaffold adapted for ingrowth of fibrochondrocytes.

16. The device of claim 1, wherein the device is a meniscal augmentation device for implantation into a segmental defect of a meniscus.

17. The device of claim 16, wherein the device an outer surface contour substantially complementary to the segmental defect of the meniscus.

18. The device of claim 16, wherein the *in vivo* outer surface of the composite of the meniscus and the device is substantially the same as that of a natural meniscus without segmental defects.

19. The device of claim 16, wherein the device is adapted for the ingrowth of meniscal fibrochondrocytes.

20. The device of claim 19, wherein the device matrix and the ingrown meniscal fibrochondrocytes support natural meniscal load forces.

21. The device of claim 16, wherein the segmental defect of the meniscus is a tear and the device is formed as a sheet sized to be inserted within the segmental defect of the meniscus.

22. The device of claim 1, wherein the device is a prosthetic intervertebral disc, the device being adapted to have *in vivo* an outer surface contour substantially the same as that of a natural intervertebral disc.

23. The device of claim 22, wherein the device matrix establishes a bioresorbable scaffold adapted for ingrowth of vertebral fibrochondrocytes.

24. The device of claim 22, wherein the device matrix and the ingrown fibrochondrocytes support vertebral tensile forces.

25. The device of claim 1, wherein the device is a prosthetic ligament comprising a plurality of substantially aligned, elongated filaments.

26. The device of claim 25, wherein the filaments in the device matrix establish a bioresorbable scaffold adapted for ingrowth of ligament fibroblasts.

27. The device of claim 25, wherein the device matrix and the ingrown fibroblasts support natural ligament tensile forces.

28. The device of claim 25,

(a) wherein the fibrils are present in the matrix at a concentration of about 75 to 100% by dry weight, and

(b) wherein polysaccharide molecules in the matrix are present at a concentration of about 0 to 25% by dry weight.

29. The device of claim 25, wherein the polysaccharide molecules are selected from the group consisting of chondroitin 4-sulfate, chondroitin 6-sulfate, keratan sulfate, dermatan sulfate, heparan sulfate, heparin, alginic acid, chitosan, hyaluronic acid, and mixtures thereof.

30. The device of claim 1, wherein the device is a prosthetic articular cartilage device adapted to have an *in vivo* outer surface contour substantially the same as that of natural articular cartilage.

31. The device of claim 30, wherein the device matrix has a pore size in the approximate range of about 100 microns to about 400 microns.

32. The device of claim 1 wherein the matrix material comprises fibers selected from the group consisting of collagen, elastin, and reticulin, analogs thereof, and mixtures thereof.

33. The device of claim 32, wherein the collagen is selected from the group consisting of Type I collagen, Type II collagen, and a combination thereof.

34. The device of claim 1, wherein the matrix material comprises polysaccharides.

35. The device of claim 1, wherein the matrix material comprises glycosaminoglycan (GAG) molecules.

36. The device of claim 35, wherein the glycosaminoglycan molecules comprise a glycosaminoglycan molecule selected from the group consisting of chondroitin 4-sulfate; chondroitin 6-sulfate; keratin sulfate; dermatan sulfate; and hyaluronic acid.

37. The device of claim 1, wherein the device matrix has a pore size substantially in the range 10-50 microns.

38. The device of claim 1, wherein the device matrix has a pore size in the approximate range of greater than 50 microns to less than about 500 microns.

39. The device of claim 1, wherein the device matrix has a density of about 0.07 to 0.50 gram matrix per cubic centimenter.

40. The device of claim 1, wherein the device matrix has a density of about 0.10 to about 0.25 gram matrix per cubic centimeter.

41. The device of claim 1, wherein the device matrix has an intrafibrillary and interfibrillary space of about 2 to 25 cubic centimeters per gram matrix material.

42. The device of claim 1, wherein the device matrix has an intrafibrillary and interfibrillary space of about 2 to 14 cubic centimeters per gram matrix.

43. The device of claim 1, wherein the matrix material further comprises one or more growth factors.

44. The device of claim 43, wherein the growth factor is transforming growth factor-α, transforming growth factor-β, fibroblast growth factor, epidermal growth factor, platelet derived growth factor, or combinations thereof.

45. The device of claim 1, wherein the matrix material further comprises an adhesion molecule.

46. The device of claim 45, wherein the adhesion molecule is fibronectin, chondronectin, osteonectin, or combinations thereof.

47. The device of claim 1, wherein the matrix material is polyethylene glycol-treated.

48. The device of claim 1, wherein the matrix material is produced by:

(a) removing at least a portion of a soft tissue from a non-human vertebrate animal to provide a matrix material for the prosthetic device;

(b) washing the matrix material in water and alcohol;

(c) subjecting the matrix material to a cellular disruption treatment; and

(d) digesting the matrix material with a proteoglycan-depleting factor to remove substantially a plurality of proteoglycans from the matrix material,

whereby the matrix material of the prosthetic device is substantially reduced in proteoglycans.

49. The device of claim 48, wherein the proteoglycan-depleting factor is selected from the group consisting of chondroitinase ABC, hyaluronidase, chondroitin AC II lyase, keratanase, trypsin and fibronectin fragment.

50. The device of claim 1, wherein the prosthetic device is sterilized.

51. The device of claim 1, wherein the device has a substantially wedge shape, having a wide central region between two narrow distal tip regions.

52. The device of claim 1,

(a) wherein the matrix has the shape of a circumferentially extending wedge having a central region and a region peripheral thereto, and spanning a predetermined angle greater than 0 degrees and less than or equal to 360 degrees about the central region, and

(b) where the thickness in the central region of the wedge is less than the thickness in the peripheral region of the wedge.

53. The device of claim 52, wherein the circumferentially extending wedge is crescent-shaped, having a wide central region between two narrow distal tip regions.

54. The device of claim 52, wherein the circumferentially extending wedge spans an angle of 360 degrees.

55. The device of claim 1,

(a) wherein collagen fibers are present in the matrix material at a concentration of about 65%-98% by dry weight, and

(b) wherein glycosaminoglycan molecules are present in the matrix material at a concentration of about 1%-25% by dry weight.

56. The device of claim 1, further comprising a mesh surrounding the device matrix, the mesh being absorbable and nonimmunogenic.

57. The device of claim 30, further comprising a biocompatible conical base component including an anchor for anchoring the articular cartilage device in a complimentary aperture in cancellous bone, the base component extending from portions of the outer surface of the matrix.

58. The device of claim 57, wherein the base component is at least partially resorbable.

59. The device of claim 57, wherein the base component includes a plurality of circumferentially extending ridges.

60. The device of claim 57, wherein the base component is composed of a composite material, comprising:

(a) a dispersion of collagen and a

(b) composition which is selected from the group consisting of tricalcium phosphate, hydroxyapatite, and a combination of tricalcium phosphate and hydroxyapatite.

61. The device of claim 60, wherein the dispersion comprises about 90% by weight tricalcium phosphate and about 10% by weight collagen.

62. The device of claim 60, wherein the dispersion comprises about 90% by weight hydroxyapatite and about 10% by weight collagen.

63. A method of making a prosthetic device for implantation into a subject, comprising the steps of:

(a) obtaining a substantially immunologically-compatible matrix material, wherein the matrix material is substantially lacking a plurality of first surface carbohydrate moieties;

(b) fabricating the matrix material to form a device, wherein the device is adapted to have an *in vivo* an outer surface contour substantially the same as that of a region disposed between and connecting two of the subject's bones.

64. The method of claim 63, wherein the device is formed as a prosthetic device selected from the group consisting of a meniscal augmentation device, a device formed as a sheet sized to be inserted within the segmental defect of a meniscus, a prosthetic intervertebral disc, a prosthetic ligament and a prosthetic articular cartilage device.

65. The method of claim 63, wherein the obtaining of substantially immunologically-compatible matrix material in step (a) comprises:

(i) removing at least a portion of a soft tissue from a non-human animal to provide a matrix material;

(ii) washing the matrix material in water and alcohol;

(iii) subjecting the matrix material to a cellular disruption treatment; and

(iv) digesting the matrix material with a glycosidase,

whereby the matrix material is substantially non-immunogenic.

66. The method of claim 63, wherein the glycosidase is a galactosidase.

67. The method of claim 63, wherein the galactosidase is an α-galactosidase.

68. The method of claim 63, wherein the obtaining of substantially immunologically-compatible matrix material in step (a) comprises:

digesting the matrix material with at least one proteoglycan-depleting factor selected from the group consisting of chondroitinase ABC, hyaluronidase, chondroitin AC II lyase, keratanase, trypsin and fibronectin fragment.

69. The method of claim 63, wherein the obtaining of substantially immunologically-compatible matrix material in step (a) comprises:

adding to the matrix material with one or more agents selected from the group consisting of growth factors and adhesion molecules.

70. The method of claim 63, wherein the fabricating of the device in step (b) comprises cross-linking at least a portion of the fibers.

71. The method of claim 63, wherein the fabricating of the device in step (b) comprises fabricating a plurality of glycosaminoglycan molecules.

72. The method of claim 63, wherein the fabricating of the device in step (b) comprises:

treating the matrix material with one or more agents selected from the group consisting of growth factors and adhesion molecules.

73. The method of claim 63, wherein the fabricating of the device in step (b) comprises:

adding to the device matrix a mesh extending from portions of the outer surface of the device, the mesh being resorbable and biocompatible.

74. The method of claim 63, wherein the fabricating of the device in step (b) comprises:

(i) providing a plurality of essentially pure glycosidase-treated fibers of a polymeric connective tissue-type component;

(ii) cutting the fibers into segments shorter than the fibers to form fibrils;

(iii) aggregating the fibrils into a plurality of elongated filaments;

(iv) contacting the filaments with a cross-linking reagent for a time sufficient to cross-link at least a portion of the fibrils within the filaments, whereby each filament forms a dry, porous, volume matrix; and

(v) aligning a plurality of the filaments in mutually adjacent relationship, the aligned filaments forming a prosthetic ligament.

75. The method of claim 63, wherein the fabricating of the device in step (b) comprises:

fabricating a prosthetic meniscus comprising a dry porous matrix of biocompatible glycosidase-treated fibers, such that the fabricated prosthetic meniscus assumes the shape of a native meniscus when implanted into a meniscus of a subject.

76. The method of claim 63, wherein the fabricating of the device in step (b) comprises:

(i) placing a plurality of biocompatible glycosidase-treated fibers into a mold, the mold defining a shape for a meniscal prosthesis;

(ii) subjecting the fibers to a first and a second cycle of freezing and thawing;

(iii) contacting the fibers with a chemical cross-linking agent such that the fibers assume the shape of the mold; and

(iv) lyophilizing the cross-linked fibers.

77. The method of claim 76, wherein the placing in step (i) comprises:

orienting glycosidase-treated fibers of the matrix material substantially circumferentially by compressing the fibers in the mold with a piston, wherein the piston motion is substantially directed along a compression axis, while during the

compressing step the piston is rotated with respect to the mold about the compression axis.

78. The method of claim 76, wherein the placing in step (i) comprises:
orienting the fibers substantially radially.

79. The method of claim 76, wherein the subjecting in step (ii) further comprises the step of compressing the fibers prior to the second cycle of freezing and thawing.

80. A method for regenerating tissue in a subject, comprising:
(a) obtaining a prosthetic device comprising a biocompatible glycosidase-treated matrix material, and
(b) implanting the device into the vertebrate subject in a region disposed between and connecting two of the subject's bones, such that the device matrix establishes an at least partially bioresorbable scaffold adapted for ingrowth of cells selected from the group consisting of fibrochondrocytes, fibroblasts, or chondrocytes.

81. The method of claim 80, wherein the subject is a human.

82. The method of claim 80,
(a) wherein the region disposed between and connecting two of the subject's bones is a segmental defect in a meniscus in a subject;
(b) wherein the device is a prosthetic meniscus device formed such that the device has an outer surface contour substantially complementary to the segmental defect in the meniscus; and
(c) wherein the device establishes a bioresorbable scaffold adapted for ingrowth of meniscal fibrochondrocytes.

83. The method of claim 80,

(a) wherein the region disposed between and connecting two of the subject's bones is a tear of the meniscus; and

(b) wherein the device is formed as a sheet sized to be inserted into the tear.

84. The method of claim 80,

(a) wherein the region disposed between and connecting two of the subject's bones is a segmental defect in a meniscus in a subject;

(b) wherein the device is a meniscal augmentation device formed such that the *in vivo* outer surface of the composite of the device and the meniscus is substantially the same as natural meniscus without a segmental defect; and

(c) wherein the device establishes a bioresorbable scaffold adapted for ingrowth of meniscal fibrochondrocytes.

85. The method of claim 80,

(a) wherein the region disposed between and connecting two of the subject's bones is an intervertebral region;

(b) wherein the device is a prosthetic intervertebral disc adapted to have *in vivo* an outer surface contour substantially the same as that of a natural intervertebral disc; and

(c) wherein the device establishes a bioresorbable scaffold adapted for ingrowth of vertebral fibrochondrocytes.

86. The method of claim 80,

(a) wherein the region disposed between and connecting two of the subject's bones is a joint;

(b) wherein the device is a prosthetic articular cartilage device adapted to have an *in vivo* outer surface contour substantially the same as that of natural articular cartilage; and

(c) wherein the device establishes a bioresorbable scaffold adapted for ingrowth of articular chondrocytes.

87. The method of claim 81, further comprising the step of:

anchoring the device in a complementary aperture in cancellous bone by a base component extending from portions of the outer surface of the device.